II. Remarks

A. Status of the Claims

Claims 75-78 have been amended without prejudice. Support for the amendments can be found, e.g., in original claims 75-78, and on page 14, lines 11-14; page 49, line 31 to page 52, line 24; page 71, line 5 to page 73, line 20; all of the original specification as filed.

New claims 79-86 were added. Support for new claim 79 can be found, e.g., on page 19, lines 16-24, of the original specification as filed. Support for new claim 80 can be found, e.g., on page 5, line 34, and page 14, lines 16-20; page 75, lines 15-17, all of the original specification as filed. Support for new claims 81 and 82 can be found, e.g., on page 15, lines 21-29, of the original specification as filed. Support for new claim 83 can be found, e.g., on page 5, lines 30-31. Support for new claim 84 can be found e.g., on page 5, lines 8-12, of the original specification as filed. Support for new claims 85 and 86 can be found, e.g., on page 13, lines 5-22, of the original specification as filed.

Claims 1-74 were previously cancelled without prejudice.

Claims 75-86 are now pending.

Applicants submit that no new matter has been added by virtue of this amendment.

B. Claims Rejections- 35 U.S.C. § 102

Claims 75-78 were rejected under 35 U.S.C. § 102(b) over U.S. Patent No. 4,987,136 to Kreek et al. ("the Kreek patent").

The Kreek patent describes methods "for controlling gastrointestinal dysmotility in humans by administration of opioid antagonists." See e.g., Abstract.

Amended independent claim 75 recites:

> A dosage form comprising:
> particles comprising
> (a) a therapeutically active agent consisting essentially of an opioid antagonist and
> (b) means for sequestering the opioid antagonist
> such that the opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with.

Applicants submit that the Kreek patent does not teach a dosage form comprising particles comprising "(a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the said opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75. Applicants respectfully note that, in the methods of the Kreek patent, the opioid antagonist is necessarily released, e.g., in the amounts "to treat gastroenterologic disorders." See, e.g., the Kreek patent, column 2, lines 27-35.

With regard to new claim 79, Applicants note that the Kreek patent does not teach a dosage form "wherein the ratio of the amount of antagonist released from said composition after tampering to the amount of said antagonist released from said intact composition is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of said composition in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37° C" as recited in claim 79.

With regard to new claim 80, Applicants submit that the Kreek patent does not teach a composition comprising (i) particles comprising (a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the opioid antagonist is substantially not released when administered

intact; and (ii) an opioid agonist in a releasable form, "which is separate from said particles comprising a therapeutically active agent consisting essentially of an opioid antagonist", as recited in claim 80.

With regard to new claim 83, Applicants submit that the Kreek patent does not teach a dosage form "which does not pose a risk of precipitation of withdrawal in opioid tolerant or dependent patients when the dosage form is orally administered intact" as recited in claim 83.

With regard to new claim 84, Applicants submit that the Kreek patent does not teach a dosage form "wherein the opioid antagonist is not bioavailable when the dosage form is administered intact but is bioavailable when the dosage form is tampered with" as recited in claim 84.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection.

Claims 75, 76 and 78 were rejected under 35 U.S.C. § 102(b) over WO 99/32120 to Palermo ("The Palermo publication"). The Examiner stated "Palermo (WO '120) discloses an oral dosage form of an opioid analgesic, comprising an analgesically effective amount of an opioid agonist together with an opioid antagonist ..." (emphasis added).

In response, Applicants submit that the Palermo publication does not teach a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist" as recited in amended claim 1. (emphasis added).

Applicants further submit that the Palermo publication does not teach a dosage form comprising opioid antagonist that "... is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended claim 75.

With regard to new claim 79, Applicants note that the Palermo publication does not teach a dosage form "wherein the ratio of the amount of antagonist released from said composition after tampering to the amount of said antagonist released from said intact composition is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of said composition in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37° C" as recited in claim 79.

With regard to new claim 80, Applicants submit that the Palermo publication does not teach a composition comprising (i) particles comprising (a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the opioid antagonist is substantially not released when administered intact; and (ii) an opioid agonist in a releasable form, "which is separate from said particles comprising a therapeutically active agent consisting essentially of an opioid antagonist", as recited in claim 80.

With regard to new claim 83, Applicants submit that the Palermo publication does not teach a dosage form "which does not pose a risk of precipitation of withdrawal in opioid tolerant or dependent patients when the dosage form is orally administered intact" as recited in claim 83.

With regard to new claim 84, Applicants submit that the Palermo publication does not teach a dosage form "wherein the opioid antagonist is not bioavailable when the dosage form is administered intact but is bioavailable when the dosage form is tampered with" as recited in claim 84.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection.

C. Claim Rejections – 35 U.S.C. § 103(a)

Claims 75-78 were rejected under § 103(a) over the Palermo publication. The Examiner stated "[t]he Palermo reference explicitly recognizes and teaches oral dosage forms comprising opioid agonists in combination with opioid antagonists ..." (emphasis added).

In response, Applicants submit that, for the reasons articulated above with regard to the anticipation rejection over the Palermo publication, the Palermo publication does not teach or suggest a dosage form comprising particles comprising "(a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist; such that the said opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75.

With regard to new claim 79, Applicants note that the Palermo publication does not teach or suggest a dosage form "wherein the ratio of the amount of antagonist released from said composition after tampering to the amount of said antagonist released from said intact composition is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of said composition in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37° C" as recited in claim 79.

With regard to new claim 80, Applicants submit that the Palermo publication does not teach or suggest a composition comprising (i) particles comprising (a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the opioid antagonist is substantially not released when administered intact; and (ii) an opioid agonist in a releasable form, "which is separate from said particles comprising a therapeutically active agent consisting essentially of an opioid antagonist", as recited in claim 80.

With regard to new claim 83, Applicants submit that the Palermo publication does not teach or suggest a dosage form "which does not pose a risk of precipitation of withdrawal in opioid tolerant or dependent patients when the dosage form is orally administered intact" as recited in claim 83.

With regard to new claim 84, Applicants submit that the Palermo publication does not teach or suggest a dosage form "wherein the opioid antagonist is not bioavailable when the dosage form is administered intact but is bioavailable when the dosage form is tampered with" as recited in claim 84.

Accordingly, Applicants respectfully request withdrawal of the rejection.

Claims 75-78 were rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 6,004,970 to O'Malley et al. in view of U.S. Patent No. 6,120,806 to Whitmere or the Palermo publication. The Examiner stated that "O'Malley ('970) does not teach a hydrophobic material". The Examiner relied on the Whitmere patent and the Palermo publication to cure this deficiency.

In response, Applicants respectfully note that the O'Malley patent describes treatment of nicotine dependency by administration of an opioid antagonist. See, e.g., Abstract. Applicants submit that the O'Malley patent does not teach or suggest "... means for sequestering the opioid antagonist such that the said opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75.

Applicants further submit that neither the Whitmere patent nor the Palermo publication teach or suggest a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the said opioid antagonist is substantially

not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75.

Accordingly, Applicants submit that neither the Whitmere patent nor the Palermo publication cures the deficiencies of the O'Malley patent. Therefore, Applicants submit that the combination of the cited references even if properly combinable (a position which is traversed), does not teach or suggest each and every element of the present claims. In particular, the combination of the cited references, when considered as a whole, does not teach or suggest a dosage form comprising particles comprising "(a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the said opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75.

Applicants further submit that the combined teachings of the cited references would not have prompted one skilled in the art to modify the teachings of the cited references to arrive at a dosage form comprising particles comprising "(a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the said opioid antagonist is substantially not released when the dosage form is orally administered intact, as compared to the dosage form that has been tampered with" as recited in amended independent claim 75.

MPEP states that "[i]f proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984)." See, e.g., MPEP, Section 2143.01.

Applicants submit that combining the O'Malley patent together with the Palermo publication, would not have suggested to one skilled in the art a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist." Applicants respectfully note that the "therapeutically active agent consisting

essentially of an opioid antagonist" language in claim 75 excludes the presence of the opioid agonist in the particles of antagonist of claim 75, and, therefore, would render the Palermo publication unsuitable for its intended purpose- e.g., to combine an opioid agonist with an opioid antagonist such that "at least a two-step extraction process" is required to separate the opioid antagonist from the opioid agonist. Therefore, Applicants submit that the combination of the O'Malley patent and the Palermo publication would not have prompted one skilled in the art to arrive at a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist". See, e.g., MPEP, Section 2143.01. Accordingly, Applicants respectfully request withdrawal of the rejection.

Applicants further submit that the combination of the O'Malley patent and the Whitmire patent also would not have suggested to one skilled in the art a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist" as recited in claim 75. Applicants note that the Whitmire patent, when considered as a whole, mandates the presence of cyanamide in the formulations described therein. See e.g., Abstract. However, Applicants submit that the "therapeutically active agent consisting essentially of an opioid antagonist" language in claim 75 excludes the presence of the cyanamide, an essential element of the Whitmere formulations, in the particles of claim 75. Therefore, Applicants submit that one skilled in the art would not have modified the combined teachings of the O'Malley patent and the Whitmire patent to arrive at a dosage form comprising particles comprising "a therapeutically active agent consisting essentially of an opioid antagonist" as recited in claim 75, e.g., because this will render the Whitmire patent unsatisfactory for its intended purpose- e.g., administration of cyanamide in a manner described in the Whitmire patent. See, e.g., MPEP, Section 2143.01. Accordingly, Applicants request withdrawal of the rejection.

With regard to new claim 79, Applicants note that the combination of the cited references does not teach or suggest a dosage form "wherein the ratio of the amount of antagonist released from said composition after tampering to the amount of said

antagonist released from said intact composition is about 4:1 or greater, based on the in-vitro dissolution at 1 hour of said composition in 900 ml of Simulated Gastric Fluid using a USP Type II (paddle) apparatus at 75 rpm at 37° C" as recited in claim 79.

With regard to new claim 80, Applicants submit that the combination of the cited references does not teach or suggest a composition comprising (i) particles comprising (a) a therapeutically active agent consisting essentially of an opioid antagonist and (b) means for sequestering the opioid antagonist such that the opioid antagonist is substantially not released when administered intact; and (ii) an opioid agonist in a releasable form, "which is separate from said particles comprising a therapeutically active agent consisting essentially of an opioid antagonist", as recited in claim 80.

With regard to new claim 84, Applicants submit that the combination of the cited references does not teach or suggest a dosage form "wherein the opioid antagonist is not bioavailable when the dosage form is administered intact but is bioavailable when the dosage form is tampered with" as recited in claim 84.

For the foregoing reasons, Applicants respectfully request withdrawal of the rejection.

III. Conclusion

An early and favorable action on the merits is earnestly solicited. According to currently recommended Patent Office policy the Examiner is requested to contact the undersigned in the event that a telephonic interview will advance the prosecution of this application.

Respectfully submitted,
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